



Long-term projections of temperature-related mortality risks for ischemic stroke, hemorrhagic stroke, and acute ischemic heart disease under changing climate in Beijing, China

Tiantian Li^{a,*}, Radley M. Horton^b, Daniel A. Bader^b, Fangchao Liu^c, Qinghua Sun^a, Patrick L. Kinney^d

^a National Institute of Environmental Health, Chinese Center for Disease Control and Prevention, Beijing, China

^b Center for Climate Systems Research, Columbia University, New York, USA

^c Fuwai Hospital, National Center for Cardiovascular Disease, Chinese Academy of Medical Sciences and Peking Union Medical College, China

^d Department of Environmental Health, Boston University School of Public Health, Boston, USA

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ABSTRACT

Background: Changing climates have been causing variations in the number of global ischemic heart disease and stroke incidences, and will continue to affect disease occurrence in the future.

Objectives: To project temperature-related mortality for acute ischemic heart disease, and ischemic and hemorrhagic stroke with concomitant climate warming.

Methods: We estimated the exposure-response relationship between daily cause-specific mortality and daily mean temperature in Beijing. We utilized outputs from 31 downscaled climate models and two representative concentration pathways (RCPs) for the 2020s, 2050s, and 2080s. This strategy was used to estimate future net temperature along with heat- and cold-related deaths. The results for predicted temperature-related deaths were subsequently contrasted with the baseline period.

Results: In the 2080s, using the RCP8.5 and no population variation scenarios, the net total number of annual temperature-related deaths exhibited a median value of 637 (with a range across models of 434–874) for ischemic stroke; this is an increase of approximately 100% compared with the 1980s. The median number of projected annual temperature-related deaths was 660 (with a range across models of 580–745) for hemorrhagic stroke (virtually no change compared with the 1980s), and 1683 (with a range across models of 1351–2002) for acute ischemic heart disease (a slight increase of approximately 20% compared with the 1980s). In the 2080s, the monthly death projection for hemorrhagic stroke and acute ischemic heart disease showed that the largest absolute changes occurred in summer and winter while the largest absolute changes for ischemic stroke occurred in summer.

Conclusions: We projected that the temperature-related mortality associated with ischemic stroke will increase dramatically due to climate warming. However, projected temperature-related mortality pertaining to acute ischemic heart disease and hemorrhagic stroke should remain relatively stable over time.

1. Introduction

Cardiovascular diseases (CVD) have represented a major global health concern since the 21st century and they are currently the leading cause of non-communicable deaths (Alwan et al., 2011). In 2013, cardiovascular deaths accounted for almost a third of all deaths globally (17.3 million deaths). Moreover, the annual CVD mortality is projected to reach 22.2 million by 2030 (Alwan et al., 2011). Specifically, ischemic heart disease, ischemic stroke, and hemorrhagic stroke continue

to cause the greatest incidence of cardiovascular and circulatory deaths in most countries, with 8.14 million, 3.27 million, and 3.17 million deaths in 2013, respectively (Alwan et al., 2011). A report published by WHO indicated that approximately 80% of the cardiovascular deaths in 2003 occurred in developing countries. A relatively large proportion of these cases occurred in China (Aje and Miller, 2009). In China, the prevalence of CVD has risen sharply, and between 1990 and 2013, the number of CVD deaths dramatically increased, from 2.5 million to 3.7 million. Notably, the overall health profile has also changed

* Corresponding author at: National Institute of Environmental Health, Chinese Center for Disease Control and Prevention, No.7, Panjiayuan Nanli, Chaoyang District, Beijing 100021, China.

E-mail address: tiantianli@gmail.com (T. Li).

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substantially since 1990. In 1990, stroke and ischemic heart disease were ranked as the 2nd and 7th leading causes of death, respectively. In 2013, these two diseases became the two leading causes of loss of life in China. Indeed, together they accounted for 15.2% of disability adjusted life years (DALYs) (Yang et al., 2013). Indeed, ischemic heart disease, ischemic stroke, and hemorrhagic stroke accounted for over 80% of all CVD deaths in 2013 (Zhou et al., 2016).

There are many well-defined risk factors associated with ischemic heart disease and stroke. Both heat and cold may increase the risk of cardiovascular mortality and morbidity (Braga et al., 2002; Phung et al., 2016; Turner et al., 2012; Yang et al., 2015). Indeed, recent studies have shown that temperature is a risk factor for ischemic heart disease, ischemic stroke and hemorrhagic stroke (Smith, 2011). Global average temperatures have been rising for the past half-century, and the associated trend of global warming has accelerated in recent decades. An increase in the global mean surface temperature of 0.3 °C to 4.8 °C has been projected for 2081–2100 relative to 1986–2005 (Stocker et al., 2014). The changing climate has already resulted in variations in the number of incidences of ischemic heart disease and stroke, and this pattern is likely to continue, thereby affecting the burden of diseases in the future. In order to effectively prevent an increase in the prevalence of ischemic heart disease and stroke, a strategy based upon estimating the effects of climate change on these diseases is required.

In summary, we projected the future temperature-related mortality of acute ischemic heart disease, ischemic stroke, and hemorrhagic stroke as a consequence of global warming over time. We projected temperature-related mortality for the three CVD diseases in the 2020s, 2050s, and 2080s in Beijing using 31 downscaled models and two RCPs. We also aimed to provide a nuanced approach to variation and uncertainty characterization in relation to future temperature-related mortality by incorporating a range of scenarios pertaining to both demographic and climate changes.

2. Methods

We initially estimated the exposure-response relationship between the recorded figures for daily mortality caused by ischemic stroke, hemorrhagic stroke, and acute ischemic heart disease and the daily mean temperature in Beijing. We acquired downscaled temperature projections from 31 climate models under RCP4.5 and RCP8.5. These data were then combined to estimate future net temperature along with the prevalence of heat- and cold-related deaths. The results were contrasted with the baseline period.

2.1. Exposure-response relationship

2.1.1. Data

Historical data pertaining to deaths and mean temperature values (Tmean, average of 24-hour observations) for 2008 to 2013 were collected in Beijing. Daily mortality data were acquired from the Chinese Center for Disease Control and Prevention. Daily death counts resulting from ischemic stroke (ICD-10 code: I63, total of 30,042 cases during the study period), hemorrhagic stroke (ICD-10 codes: I61, total of 26,047 cases during the study period) and acute ischemic heart disease (ICD-10 code: I20–I22, I24, total of 48,853 cases during the study period) were accumulated. Daily Tmean data and other meteorological information were acquired from the China Meteorological Data Sharing Service System for Beijing (station number: 54511). In order to incorporate the possible influence of air pollution, PM_{2.5} information from 2008 until 2012 and O₃ information from 2009 until 2011 were acquired from the Beijing Meteorological Bureau, which provides daily PM_{2.5} and O₃ concentrations from the Beijing Baolian station.

2.1.2. Statistical analysis

We implemented a Poisson regression model combined with a distributed lag non-linear model (DLNM) to evaluate the influence of

temperature on mortality (Armstrong, 2014, 2006). We controlled for the day of the week as a categorical variable and accounted for the season and long-term trends with a natural cubic spline with 7 df/year for time, as the estimated effects of temperature were stabilized.

The exposure-response curve was modeled with a natural cubic spline with three internal knots placed at equally spaced values, and the lag-response curve with a natural cubic spline with the three internal knots placed at equally spaced values in the log scale. We selected a lag of 14 days to model the effects of temperature on mortality since previous studies implied that the effects of temperature on heat typically display lag effects, which potentially lead to mortality displacement (Braga et al., 2002; Guo et al., 2011). The minimum mortality risk temperatures (MMT) of 23.6 °C, 24.9 °C, and 23.8 °C for ischemic stroke, hemorrhagic stroke, and acute ischemic heart disease, respectively, were derived from the overall cumulative exposure-response association and used as the reference temperatures to calculate relative risks. The analyses were performed using R Statistical Software (version 3.2.3) and the DLNM package.

2.2. Future temperature projections

Future temperature projections were developed using downscaled outputs from 31 global scale general circulation models (GCMs) (implemented in the Intergovernmental Panel on Climate Change Fifth Assessment report) in conjunction with two representative concentration pathways (Van Vuuren et al., 2011).

The fifth Intergovernmental Panel on Climate Change (IPCC) report introduced a group of new scenarios termed RCPs. The scenarios are the result of contributions from integrated assessment modelers, climate modelers, terrestrial ecosystem modelers, and emission inventory experts (Stocker et al., 2014; Van Vuuren et al., 2011). Two RCP scenarios were chosen during this study: RCP4.5 represents a medium emission scenario and RCP8.5 alludes to a high emission scenario (Van Vuuren et al., 2011). RCP4.5 has been described as a stabilization scenario in which the total radiative forcing is stabilized shortly after 2100, without overshooting the long-run radiative forcing target level (Van Vuuren et al., 2011). RCP8.5 differs by incorporating increasing greenhouse gas emissions over time, which leads to a forcing level near the 90th percentile of the baseline CO₂ emissions range (Moss et al., 2008).

The climate model outputs from the WCRP CMIP5 multi-model dataset (<http://cmip-pcmdi.llnl.gov/cmip5/>) (Taylor et al., 2012) were further downscaled to 1/8-degree resolution with bias-correction and spatial disaggregation. The method used here was also described in a previous study (Li et al., 2016). The 31 resultant temperature projections for daily Tmean values from 2010 to 2099 are based on three 30-year time intervals (the 31 GCMs are detailed in Table S2), which include the 2020s (2010–2039), the 2050s (2040–2069), and the 2080s (2070–2099). The 1980s (1970–1999) were used as a baseline interval. The baseline period in this study is defined as the climatology over 30 years (1970–1999 mean) using a historical run (1850–2005) in CMIP5 (rather than a particular year). This approach has been widely adopted for temperature projections in IPCC5. In order to smooth out and minimize the role of unpredictable natural variability the baseline period was composed of 30-year periods. We also included a near-term period from the 2020s (2010–2039). It was not possible to use a base period later than the 1990s (1980–2009) without having an overlap between the baseline and future periods (this was deemed undesirable). In order to ensure consistency with other studies we chose the 1980s (instead of the 1990s) as a base period (Li et al., 2013, 2015, 2016).

2.3. Population

Population data for Beijing in 2010 was acquired from the Beijing Municipal Bureau of Statistics (Bureau, 2013). Two population projection scenarios were used to estimate the number of deaths in the

2020s, 2050s, and 2080s. In the “no change” scenario, the population and composition of the population were fixed at the population number for 2010 across the projection period. For the “population variation” scenario, we implemented the low, medium, and high variant scenarios of population growth for China developed by the United Nations (United Nations, Department of Economic and Social Affairs, 2014). Under the low variant scenario, fertility is projected to remain 0.5 children below the fertility in the medium variant over most of the projection period. Under the high variant, fertility is projected to remain 0.5 children above the fertility in the medium variant over most of the projection period. Under the medium variant, total fertility in all countries is assumed to converge eventually towards a level of 1.85 children per woman (United Nations, Department of Economic and Social Affairs, 2014). Baseline cause-specific mortality rates for 2010, which excluded deaths attributable to external causes, were obtained from the Chinese Center for Diseases Control and Prevention. The baseline cause-specific mortality rates were kept constant in our projection.

2.4. Mortality projection

Projected mortality impacts were estimated using the modeled daily Tmean. The change in cause-specific mortality was calculated relative to MMT for the heat effect over a 24-hour-period (with the Tmean being greater than MMT). Conversely, the change in cause-specific mortality was calculated relative to MMT for the cold effect over a 24-hour-period (with the Tmean being lower than MMT). Daily additional heat-related deaths were calculated as follows:

$$\Delta \text{Mortality} = Y_0 \times \text{ERC} \times \text{POP} \quad (1)$$

where $\Delta \text{Mortality}$ is the daily temperature-related cause-specific additional deaths, Y_0 represents the baseline daily cause-specific mortality rate (per 100,000 people), and POP is the population. ERC is the attributable percentage variation in mortality for a specified variation in temperature, derived from the calculated relative risk at each temperature from the statistical evaluation of observed data as described above.

We calculated temperature-related daily deaths in this manner for each interval (1980s, 2020s, 2050s, and 2080s), and then calculated the average number of annual temperature-related deaths. In addition, we calculated the percentage change in the number of annual average deaths from the 1980s to the specified future periods.

2.5. Sensitivity analyses

Sensitivity analyses for the exposure-response relationship evaluated the potential modifications pertaining to modeling choices, exposure metrics, and air pollution (PM_{2.5} and ozone).

2.6. Uncertainty analyses

The ANOVA-type estimation of variance components (VC) method was used for understanding the uncertainty influence of different factors (including RCPs, GCMs and population scenarios) on temperature-related mortality projection. The analyses were conducted using R Statistical Software (version 3.2) and the VCA package.

3. Results

Fig. 1 shows the overall cumulative exposure-response curve representing the relationship between daily mean temperatures and mortalities caused by ischemic stroke, hemorrhagic stroke, and acute ischemic heart disease. The curves are at lag 0–14 with the MMT at 23.6 °C, 24.9 °C, and 23.8 °C for ischemic stroke, hemorrhagic stroke, and acute ischemic heart disease, respectively. The different causes mediate the shape of the curve. All of the three causes are predicted to

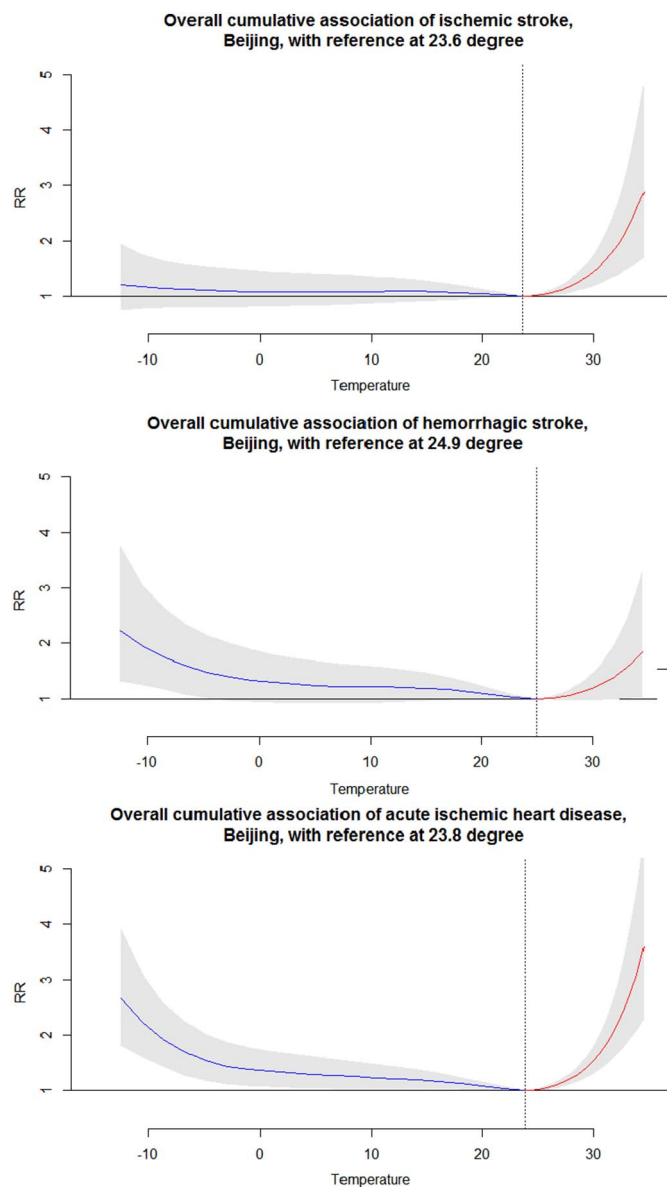


Fig. 1. Exposure-response curves for temperature-related mortality of ischemic stroke, hemorrhagic stroke, and acute ischemic heart disease.

respond to the heat effect, with the largest heat effect exhibited by acute ischemic heart disease. The mortality of hemorrhagic and acute ischemic heart disease increased with the cold effect while ischemic stroke exhibited a limited response to the cold effect. Temperatures above the MMT were associated with the excess cause-specific mortality pertaining to heat, and temperatures below the MMT were associated with the excess cause-specific mortality pertaining to cold. Results from the sensitivity analysis of the temperature and mortality relationship pertaining to the three causes are presented in Tables S2–S10. Results were not substantially affected in the different sensitivity models. We examined different cumulative lags, consistent with recent studies (Guo et al., 2014); the effect estimates of other lag structures (0–7 days, 0–21 days, and 0–28 days) were not dissimilar to those at lag 0–14 for the three causes (Supplementary Tables S2, S5, and S8).

Fig. 2 represents the projected distribution of net, heat- and cold-related annual acute deaths for ischemic stroke, hemorrhagic stroke, and acute ischemic heart disease from the 1980s to the 2080s under both RCP4.5 and RCP8.5 with the population held constant at the 2010 level (no population change). Results are reported separately for different causes. The number of net annual temperature-related deaths is

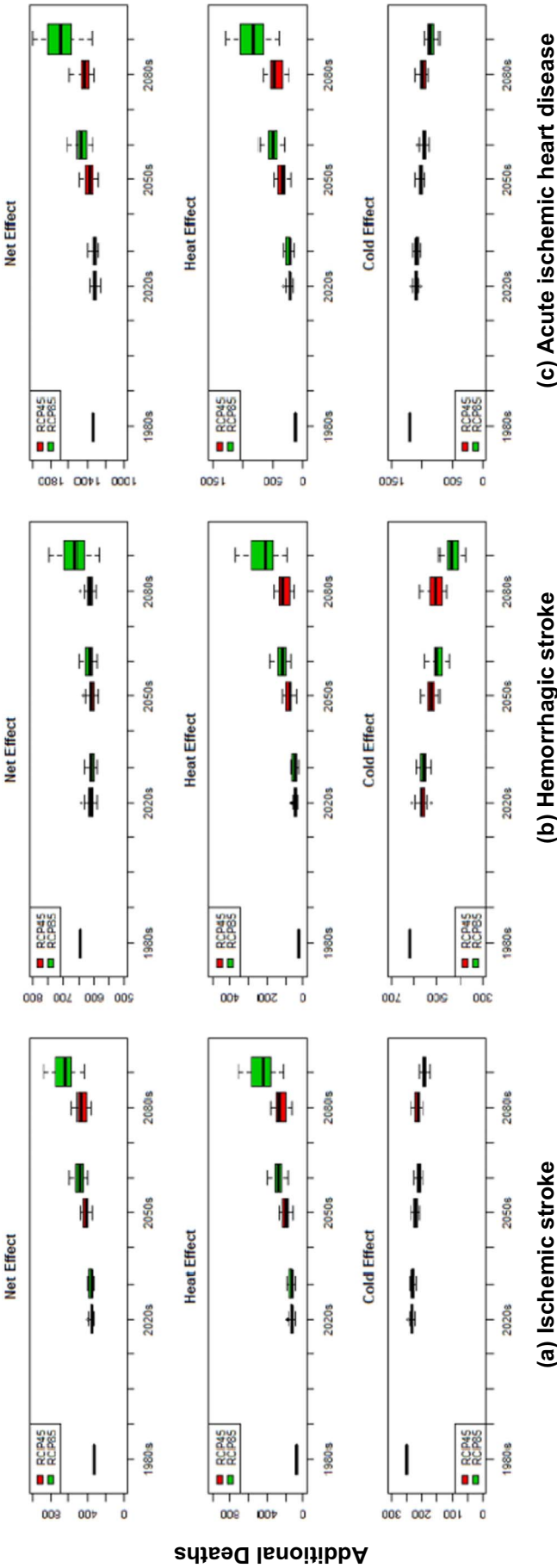


Fig. 2. Distribution of net, heat-, and cold-related annual acute deaths for ischemic stroke, hemorrhagic stroke, and ischemic heart disease in the 1980s, 2020s, 2050s, and 2080s using 31 climate models and the RCP4.5 and RCP8.5 scenarios.

projected to increase on an annual basis for all three diseases. The highest number of net annual temperature-related deaths occurred for acute ischemic heart disease followed by deaths caused by ischemic stroke and hemorrhagic stroke. Net and heat-related annual deaths for all three causes using the RCP8.5 scenario increased more rapidly from the 1980s to 2080s compared with those using the RCP4.5 scenario, while cold-related annual deaths decreased more rapidly using the RCP8.5 scenario. In the 2080s using RCP8.5, the net median number of annual temperature-related deaths was 637 (with a range across models of 434–874) for ischemic stroke, 660 (with a range across models of 580–745) for hemorrhagic stroke, and 1683 (with a range across models of 1351–2002) for acute ischemic heart disease. To further understand the correlation between the temperature-related mortality projection and exposure-response function, we also changed the confidence intervals for the central estimate of exposure-response relationship to 95% to represent the uncertainty of the exposure-response function. All of the projections for the three cause-specific diseases from the 31 models are shown in Figs. S1 to S3. For all three diseases, the heat projections were not grossly affected by the exposure-response function. Conversely, both the cold and net projections were significantly affected by the exposure-response function.

Fig. 3 shows the median percentage change of net (heat and cold) temperature-related annual cause-specific deaths in the 2020s, 2050s, and 2080s using the RCP4.5 and RCP8.5 scenarios. The number of ischemic stroke deaths increased dramatically compared with the other two causes. In the 2080s using RCP8.5, temperature-related ischemic stroke deaths increased by approximately 100% compared with the 1980s. Hemorrhagic stroke showed a different profile with nearly no alterations to incidence in future analyzed intervals. The number of deaths due to acute heart disease increased slightly with more than a 20% increase compared with the 1980s.

The percentage change in the median number of monthly temperature-related cause-specific deaths from the 1980s is shown in

Supplementary Fig. S4. In the 2080s under RCP8.5, all three causes of death exhibited the largest changes compared with the baseline period. Fig. 4 shows the number of median monthly temperature-related deaths for the three causes and the percentage variation from the 1980s to the 2080s using both the RCP4.5 and RCP8.5 scenarios. In the 2080s, the monthly death projection for hemorrhagic stroke and acute ischemic heart disease showed that the largest absolute number of deaths occurred in the summer and the winter while the largest number of deaths for ischemic stroke occurred in the summer. The percentage increases for monthly death projections for all three causes in the 2080s were greatest in the summer months with the maximum increases occurring in August.

Projected median annual temperature-related deaths for all three causes with three population variation scenarios and no population changes are shown in Fig. S5. Under the high population variation scenario, temperature-related deaths due to the three causes increased from the 1980s to the 2080s under both RCP4.5 and RCP8.5, and the projected values are greater than the projection for the no population change scenario. Apart from the number of temperature-related deaths caused by ischemic stroke under RCP8.5, the projection based on the other scenarios showed a decreasing trend in the 2080s. Median annual temperature-related deaths and percentage changes for the three causes relative to the 1980s using the population high variation scenario and RCP8.5 are shown in Fig. 5. Projected impacts increased the median for ischemic stroke by 137%, while the same impacts increased the median for acute ischemic heart disease by 55%, and hemorrhagic stroke by 26% in the 2080s compared with the 1980s.

Results from the uncertainty analysis of temperature-related cause-specific mortality are presented in Fig. S6. For all 3 cause-specific mortality projections, the population scenarios were attributed the highest uncertainty, followed by the RCPs.

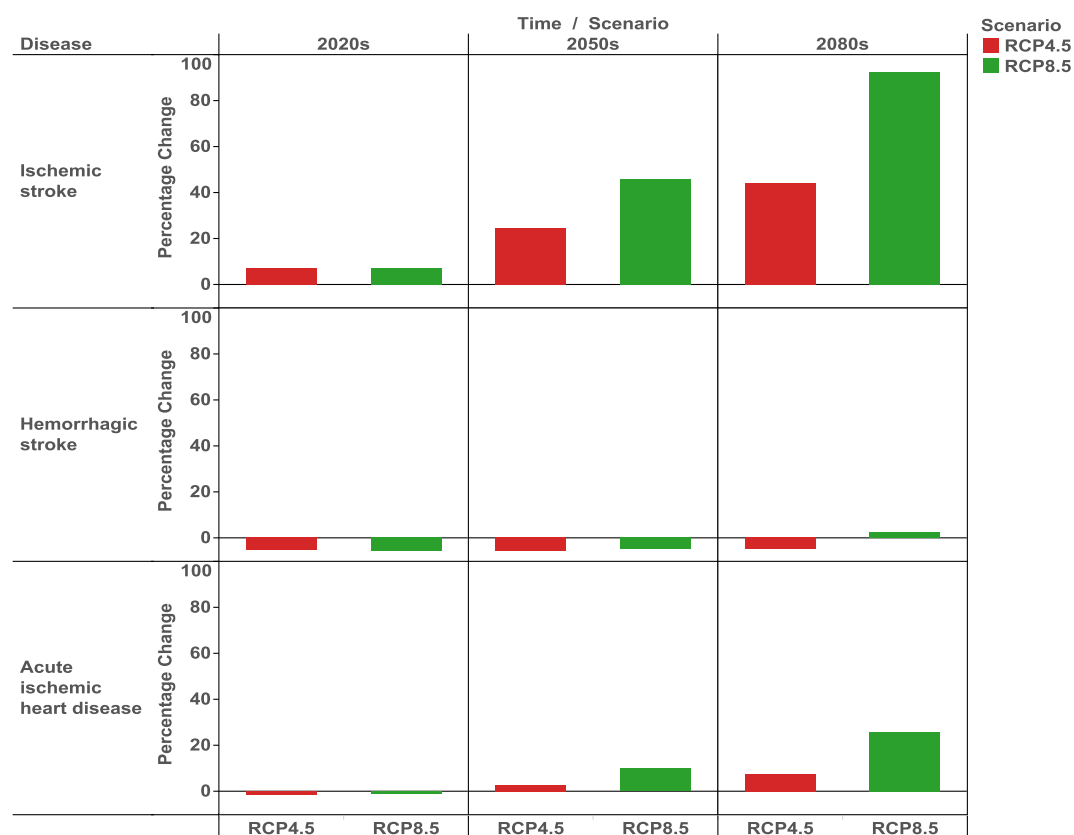


Fig. 3. Median percentage change in net temperature-related annual cause-specific deaths in the 2020s, 2050s, and 2080s using the RCP4.5 and RCP8.5 scenarios.

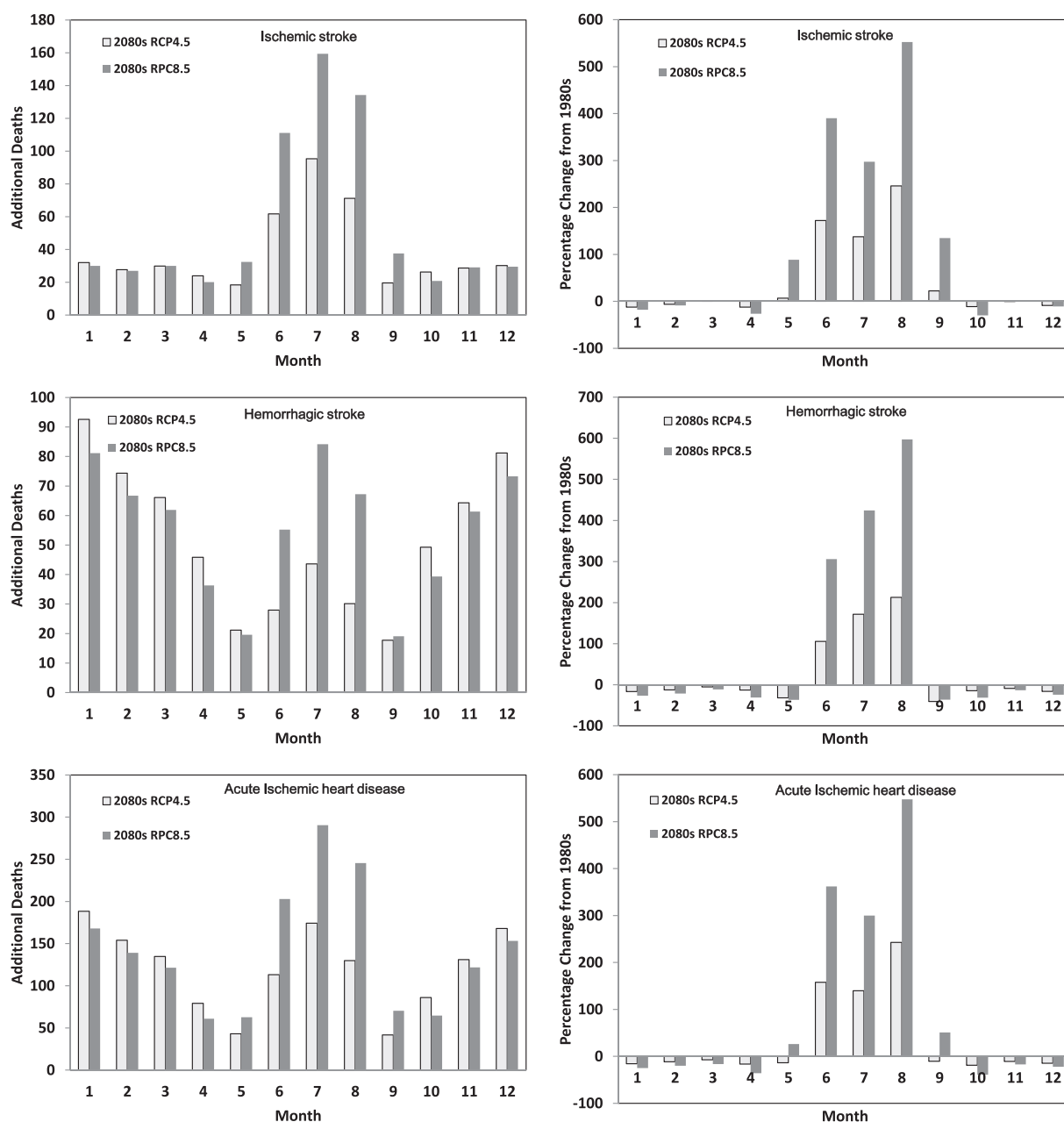


Fig. 4. Median monthly temperature-related cause-specific deaths and percentage change in the 2080s using the RCP4.5 and RCP8.5 scenarios.

4. Discussion

To the best of our knowledge, this study is the first-ever projection study to investigate the temperature-related mortality for three major CVDs using a full range of available climate models, as well as population and RCP scenarios over the 21st century. We determined variations in the number of future annual temperature-related deaths for the three diseases, and evaluated how heat- and cold-related mortalities are affected in a changing climate. We also showed the future potential monthly variations of temperature-related deaths for the three diseases. We observed that temperature-related mortality (caused by climate warming) for ischemic stroke is increasing dramatically. There was a relatively smaller projected increase in temperature-related deaths caused by acute ischemic heart disease, while hemorrhagic stroke was projected to be relatively stable over time. Our findings provide a platform for countries implementing public health intervention policies for stroke and acute ischemic heart disease, and deliver the first insight

into the potential problems caused by climate change in relation to circulation disease occurrence.

Numerous studies have shown that stroke mortality is affected by relatively hot and cold environmental temperature effects (Gomes et al., 2015; Lian et al., 2015). However, there have been a limited number of studies pertaining to the relationship between temperature and ischemic or hemorrhagic stroke. We observed a relatively greater heat effect for ischemic stroke and a relatively greater cold effect for hemorrhagic stroke; these results are consistent with previous limited studies (Lian et al., 2015). Previous studies have shown that both extreme heat and cold effect ischemic heart disease occurrence; our study found similar results (Guo et al., 2013). A previous meta-analysis performed a review of 10 studies that investigated the cold effects of temperature on ischemic stroke mortality. The meta-analysis resulted in the generation of a positive effect estimate result (however, not all of the results were significant) (Lian et al., 2015). Our study showed that the mortality risk of ischemic stroke increased by 1.03% (95%CI:

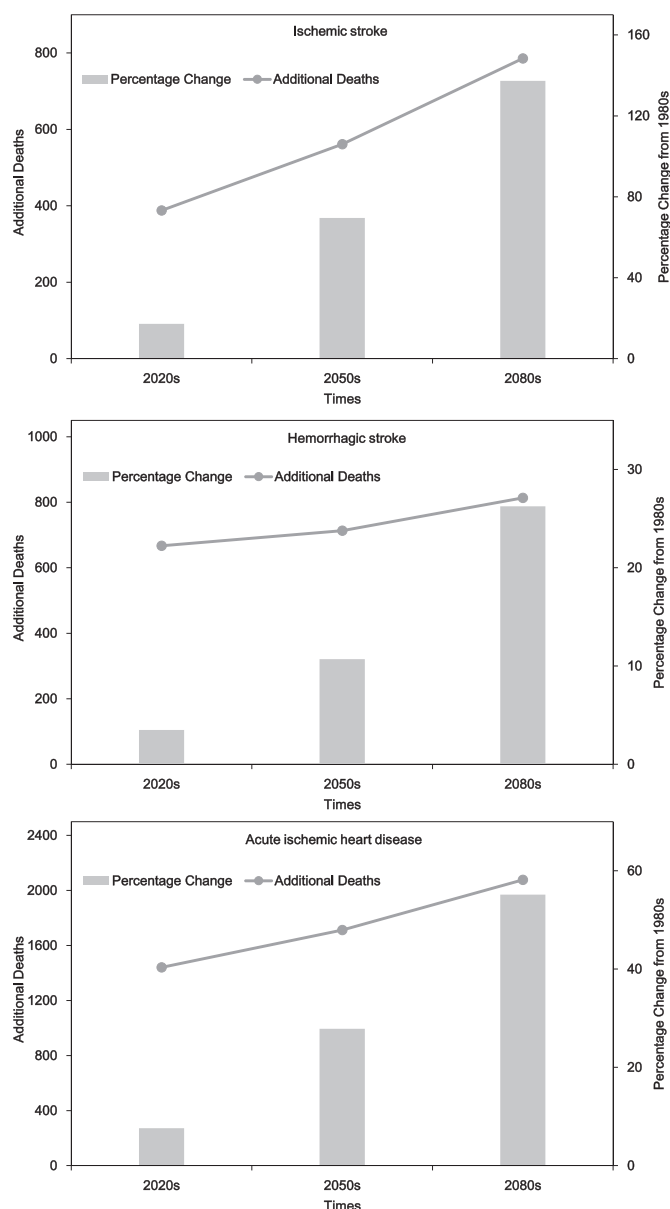


Fig. 5. Median annual temperature-related cause-specific deaths and percentage change from 1980s with the population high variation scenario using RCP8.5.

0.94–1.12%) compared with an initial 1st percentile of the temperature distribution to 5th percentile of the temperature distribution. This result is consistent with results generated in previous studies. However, some of the studies that have been performed in this field are limited due to the employment of very wide confidence intervals and very large effect estimate values (Hong et al., 2003; Hori et al., 2012). Thus, further research is required to fully elucidate the aforementioned relationship. It is interesting to note that even though a correlation between temperature and mortality caused by stroke and ischemic heart disease has been proven by many studies, studies that have attempted to elucidate the relationship between temperature and morbidity due to stroke and ischemic heart disease remain controversial (Lian et al., 2015; Phung et al., 2016; Turner et al., 2012). More studies are needed to fully explicate the relationship between temperature and morbidity due to stroke and ischemic heart disease.

Under the constant population scenario, the three diseases showed different variation trends by the end of 21st century. Temperature-related mortality showed the greatest increase for ischemic stroke incidence, followed by acute ischemic heart disease, whereas

hemorrhagic stroke incidence remained relatively stable. The increase in temperature-related mortality for ischemic stroke and acute ischemic heart disease was predominantly caused by an increase in the number of heat-related mortality incidences (as opposed to an increase in the number of cold-related mortality incidences). A similarly increasing trend for both ischemic stroke and acute ischemic heart disease may be due to similarities pertaining to the pathogenesis of atherosclerosis (Gaggini et al., 2013; Kernan et al., 2014). Because increases in the numbers of heat-related mortality incidences approximately match decreases in the number of cold-related mortality cases, the temperature-related mortality of hemorrhagic stroke showed a different profile compared with the other two disease causes. The rupture of blood vessels is the predominant symptom of pathogenesis for hemorrhagic stroke (Xia et al., 2014). It is possible that this characteristic underpins the afore-mentioned differences compared with ischemic diseases. Although the underlying mechanisms that relate temperature to cardiovascular disease occurrence are not well understood, there are multiple biological mechanisms that could potentially explain this phenomenon. Low temperatures were shown to increase blood pressure and fibrinogen concentration, induce vasoconstriction of peripheral blood vessels, and enhance platelet aggregation and sympathetic nervous system activation (Cheng and Su, 2010; Manfredini et al., 1997; McArthur et al., 2010). Meanwhile, high temperatures might impair peripheral vascular endothelial function, and increase plasmatic viscosity and cardiac output (Nawrot et al., 2005).

In 2010, China had a considerably higher relative stroke mortality rate than the rest of the world, with stroke becoming the leading cause of deaths in that year (Smith, 2011; Yang et al., 2013). Our results indicate that problems arising from stroke occurrence, especially ischemic stroke, could be more serious in China with concomitant climate change in the future. A 21-year-long observational stroke study from 1984 to 2004 in Beijing showed that the incidence rate of hemorrhagic stroke declined by 1.7% and the incidence rate of ischemic stroke increased by 8.7% (Zhao et al., 2008). As there is no published ischemic and hemorrhagic stroke mortality rate for Beijing, it is worth mentioning that our long-term projection work revealed a similar variation trend for hemorrhagic stroke and ischemic stroke, respectively, following the use of an historical observational study. We could not compare the projection trend with the historical mortality trend because no published ischemic and hemorrhagic stroke mortality transit information is available for Beijing. In 1990, ischemic heart disease was the seventh leading cause of death in China. The same disease became the second leading cause of death in 2010 (Yang et al., 2013). In addition, the mortality rate associated with ischemic heart disease increased from 8.5% in 1984 to 15.7% in 2004 (Zhao et al., 2008). The increasing temperature-related death projections for acute ischemic heart disease in the next several decades show a similar profile to historical mortality rate trends.

We considered both extreme heat and cold in our projections, thereby making it possible to analyze the full-year projections by calendar months. In the 2080s, large percentage increases in temperature-related mortality for the three diseases occurred in the summer and late spring, which is consistent with previous studies (Guo et al., 2016; Li et al., 2013). Increased awareness in related government sectors is imperative in facilitating advanced planning and policy implementation to allow countries to cope with dramatic increases in disease occurrence in summer months. The projected seasonal variations in temperature-related mortality rates due to the three diseases are substantially different for the 2080s. In the 2080s, the highest incidence of temperature-related mortality for ischemic stroke occurs in the summer, while the greatest prevalence of temperature-related mortality for hemorrhagic stroke and acute ischemic heart disease occur in both the summer and winter. This phenomenon should remind us that specific preventive measures for different diseases should be promulgated by public health authorities when planning disease control and prevention strategies.

Population changes have been increasingly considered in recent

years upon assessment of future potential health risk factors. Unfortunately, many of these studies projected only to the middle of the century and did not perform comparisons using alternative population scenarios (Hajat et al., 2014; Huang et al., 2011; Petkova et al., 2016). For countries like China, which are likely to experience large population increases in the future, integration of demographic scenarios into projections is crucially important. We observed that when high population variation and RCP8.5 scenarios were analyzed, temperature-related mortality is projected to increase by approximately 137% for ischemic stroke, 26% for hemorrhagic stroke and 55% for acute ischemic heart disease by the 2080s compared with the 1980s. The three diseases, especially ischemic stroke, displayed the largest future increases resulting from climate warming and population growth. Our work, for the first time, provides quantitative evidence from projections with and without demographic changes for the three diseases in China. This analysis is likely to be beneficial in relation to policy planning for the prevention of the three analyzed CVD diseases.

We applied downscaled outputs from 31 different GCMs and two future RCPs; this is the most comprehensive downscaling temperature projection dataset available for China. The RCPs provide specific methodological advantages compared with the previous Special Report on Emissions Scenarios (SRES) in relation to the provision of important uncertainty information for adaptation policy planning. Since a greater number of climate models were utilized for RCPs, these scenarios provide a broader range of potential outcomes compared with SRESs. This study also has clear limitations. In order to bolster the Beijing population projection analysis, we applied UN population projection results, which were developed for all of China. Beijing is a rapidly developing city with a growing population. Therefore, by using the population projection variation rate for the whole of China, there is a possibility that we are underestimating the potential temperature-related cause-specific mortality risk in Beijing. A significant limitation is that future adaptation to heat was not modeled in this study. The temperature-mortality relationship may not remain stable over time because of acclimatization (Kinney et al., 2008). Human capacity to adapt to the warm climate could increase (Petkova et al., 2014), which may result in an overestimation of the number of heat-related deaths for the three diseases in our study. Conversely, the adaptive capacity of the population to the cold may decrease in the future as extreme cold is experienced less frequently (Kinney et al., 2015); however, addressing acclimatization to the cold is a complex problem in the field of projection (Kinney et al., 2008). Therefore, it is possible that we have underestimated the number of cold-related deaths reported in this study. We maintained a constant population mortality rate for the three diseases, which means that the changes in public health status, potential improvements in CVD education, future access to healthcare, related healthcare advancements, socioeconomic status, air pollution and other factors were not considered in this study (Huang et al., 2011; Kinney et al., 2008).

A greater understanding of projected temperature-related deaths caused by ischemic stroke, hemorrhagic stroke, and acute ischemic heart disease is likely to improve our existing knowledge, and enhance current action plans to mitigate variations associated with disease occurrence caused by climate change. Future research is required to address the changing adaptive capacity of the population to extreme heat and cold; we should also strive to reduce, as much as possible, uncertainty relating to these projections. Further outcomes pertaining to specific diseases should also be explored, and a multi-center study design is highly recommended to facilitate future research.

5. Conclusions

We projected that the temperature-related mortality associated with ischemic stroke will increase dramatically due to climate warming. However, projected temperature-related mortality associated with acute ischemic heart disease and hemorrhagic stroke should remain

relatively stable over time. These findings are critical for countries involved in implementing public health intervention policies for both stroke and acute ischemic heart disease. This study provides a unique insight into the role that temperature might play in the prevalence of stroke and heart disease in the future.

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Competing financial interests

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2017.12.006>.

References

- Aje, T.O., Miller, M., 2009. Cardiovascular disease: a global problem extending into the developing world. *World J. Cardiol.* 1, 3–10. <http://dx.doi.org/10.4330/wjc.v1.i1.3>.
- Alwan, A., et al., 2011. Global, Regional, and National Age-Sex Specific All-cause and Cause-specific Mortality for 240 Causes of Death, 1990–2013: A Systematic Analysis for the Global Burden of Disease Study 2013. *World Health Organization*.
- Armstrong, B., 2006. Models for the relationship between ambient temperature and daily mortality. *Epidemiology* 17, 624–631. <http://dx.doi.org/10.1097/01.ede.0000239732.50999.8f>.
- Armstrong, A.G., 2014. *dlm: Distributed Lag Non-linear Models*.
- Braga, A.L., Zanobetti, A., Schwartz, J., 2002. The effect of weather on respiratory and cardiovascular deaths in 12 US cities. *Environ. Health Perspect.* 110, 859.
- Bureau, B.S., 2013. *Beijing Statistical Yearbook*. Chinese Statistical Publishing House, Beijing.
- Cheng, X., Su, H., 2010. Effects of climatic temperature stress on cardiovascular diseases. *Eur. J. Intern. Med.* 21, 164–167.
- Gaggini, M., Morelli, M., Buzzigoli, E., DeFronzo, R.A., Bugianesi, E., Gastaldelli, A., 2013. Non-alcoholic fatty liver disease (NAFLD) and its connection with insulin resistance, dyslipidemia, atherosclerosis and coronary heart disease. *Nutrients* 5, 1544–1560.
- Gomes, J., Damasceno, A., Carrilho, C., Lobo, V., Lopes, H., Madede, T., et al., 2015. Triggering of stroke by ambient temperature variation: a case-crossover study in Maputo, Mozambique. *Clin. Neurol. Neurosurg.* 129, 72–77. <http://dx.doi.org/10.1016/j.clineuro.2014.12.002>.
- Guo, Y., Barnett, A.G., Pan, X., Yu, W., Tong, S., 2011. The impact of temperature on mortality in Tianjin, China: a case-crossover design with a distributed lag nonlinear model. *Environ. Health Perspect.* 119, 1719–1725. <http://dx.doi.org/10.1289/ehp.1103598>.
- Guo, Y., Li, S., Zhang, Y., Armstrong, B., Jaakkola, J.J.K., Tong, S., et al., 2013. Extremely cold and hot temperatures increase the risk of ischaemic heart disease mortality: epidemiological evidence from China. *Heart* 99, 195–203. <http://dx.doi.org/10.1136/heartjnl-2012-302518>.
- Guo, Y., Gasparrini, A., Armstrong, B., Li, S., Tawatsupa, B., Tobias, A., et al., 2014. Global variation in the effects of ambient temperature on mortality: a systematic evaluation. *Epidemiology* 25, 781.
- Guo, Y., Li, S., Liu, D.L., Chen, D., Williams, G., Tong, S., 2016. Projecting future temperature-related mortality in three largest Australian cities. *Environ. Pollut.* 208, 66–73. <http://dx.doi.org/10.1016/j.envpol.2015.09.041>.
- Hajat, S., Vardoulakis, S., Heaviside, C., Eggen, B., 2014. Climate change effects on human health: projections of temperature-related mortality for the UK during the 2020s, 2050s and 2080s. *J. Epidemiol. Community Health* 68, 641–648.
- Hong, Y.-C., Rha, J.-H., Lee, J.-T., Ha, E.-H., Kwon, H.-J., Kim, H., 2003. Ischemic stroke associated with decrease in temperature. *Epidemiology* 14, 473–478. <http://dx.doi.org/10.1097/01.ede.0000078420.82023.e3>.
- Hori, A., Hashizume, M., Tsuda, Y., Tsukahara, T., Nomiya, T., 2012. Effects of weather variability and air pollutants on emergency admissions for cardiovascular and cerebrovascular diseases. *Int. J. Environ. Health Res.* 22, 416–430. <http://dx.doi.org/10.1080/09603123.2011.650155>.
- Huang, C., Barnett, A.G., Wang, X., Vaneckova, P., FitzGerald, G., Tong, S., 2011. Projecting future heat-related mortality under climate change scenarios: a systematic review. *Environ. Health Perspect.* 119, 1681–1690. <http://dx.doi.org/10.1289/ehp.1103456>.
- Kernan, W.N., Ovbiagele, B., Black, H.R., Bravata, D.M., Chimowitz, M.I., Ezekowitz, M.D., et al., 2014. Guidelines for the prevention of stroke in patients with stroke and

- transient ischemic attack a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 45, 2160–2236.
- Kinney, P.L., O'Neill, M.S., Bell, M.L., Schwartz, J., 2008. Approaches for estimating effects of climate change on heat-related deaths: challenges and opportunities. *Environ. Sci. Pol.* 11, 87–96.
- Kinney, P.L., Schwartz, J., Pascal, M., Petkova, E., Tertre, A.L., Medina, S., et al., 2015. Winter season mortality: will climate warming bring benefits? *Environ. Res. Lett.* 10, 064016. <http://dx.doi.org/10.1088/1748-9326/10/6/064016>.
- Li, T., Horton, R.M., Kinney, P.L., 2013. Projections of seasonal patterns in temperature-related deaths for Manhattan, New York. *Nat. Clim. Chang.* 3, 717–721. <http://dx.doi.org/10.1038/nclimate1902>.
- Li, T., Ban, J., Horton, R.M., Bader, D.A., Huang, G., Sun, Q., et al., 2015. Heat-related mortality projections for cardiovascular and respiratory disease under the changing climate in Beijing, China. *Sci. Rep.* 5, 11441. <http://dx.doi.org/10.1038/srep11441>.
- Li, T., Horton, R.M., Bader, D.A., Zhou, M., Liang, X., Ban, J., et al., 2016. Aging will amplify the heat-related mortality risk under a changing climate: projection for the elderly in Beijing, China. *Sci. Rep.* 6, 28161. <http://dx.doi.org/10.1038/srep28161>.
- Lian, H., Ruan, Y., Liang, R., Liu, X., Fan, Z., 2015. Short-term effect of ambient temperature and the risk of stroke: asystematic review and meta-analysis. *Int. J. Environ. Res. Public Health* 12, 9068–9088. <http://dx.doi.org/10.3390/ijerph120809068>.
- Manfredini, R., Gallerani, M., Portaluppi, F., Salmi, R., Fersini, C., 1997. Chronobiological patterns of onset of acute cerebrovascular diseases. *Thromb. Res.* 88, 451–463.
- McArthur, K., Dawson, J., Walters, M., 2010. What is it with the weather and stroke? *Expert. Rev. Neurother.* 10, 243–249.
- Moss, R.H., Nakicenovic, N., O'Neill, B.C., 2008. Towards New Scenarios for Analysis of Emissions, Climate Change, Impacts, and Response Strategies.
- Nawrot, T.S., Staessen, J.A., Fagard, R.H., Van Bortel, L.M., Struijker-Boudier, H.A., 2005. Endothelial function and outdoor temperature. *Eur. J. Epidemiol.* 20, 407–410.
- Petkova, E.P., Gasparrini, A., Kinney, P.L., 2014. Heat and mortality in New York City since the beginning of the 20th century. *Epidemiology* 25, 554.
- Petkova, E.P., Vink, J.K., Horton, R.M., Gasparrini, A., Bader, D.A., Francis, J.D., et al., 2016. Towards more comprehensive projections of urban heat-related mortality: estimates for New York City under multiple population, adaptation, and climate scenarios. *Environ. Health Perspect.* <http://dx.doi.org/10.1289/EHP166>.
- Phung, D., Thai, P.K., Guo, Y., Morawska, L., Rutherford, S., Chu, C., 2016. Ambient temperature and risk of cardiovascular hospitalization: an updated systematic review and meta-analysis. *Sci. Total Environ.* 550, 1084–1102. <http://dx.doi.org/10.1016/j.scitotenv.2016.01.154>.
- Smith, S.C., 2011. Reducing the global burden of ischemic heart disease and stroke: a challenge for the cardiovascular community and the United Nations. *Circulation* 124, 278–279. <http://dx.doi.org/10.1161/CIRCULATIONAHA.111.040170>.
- Stocker, T.F., Qin, D., Plattner, G.-K., Tignor, M., Allen, S.K., Boschung, J., et al., 2014. *Climate Change 2013: The Physical Science Basis*. Cambridge University Press, Cambridge, UK, and New York.
- Taylor, K.E., Stouffer, R.J., Meehl, G.A., 2012. An overview of CMIP5 and the experiment design. *Bull. Am. Meteorol. Soc.* 93, 485.
- Turner, L.R., Barnett, A.G., Connell, D., Tong, S., 2012. Ambient temperature and cardiorespiratory morbidity: asystematic review and meta-analysis. *Epidemiology* 23, 594–606. <http://dx.doi.org/10.1097/EDE.0b013e3182572795>.
- United Nations, Department of Economic and Social Affairs, 2014. World population prospects: the 2012 revision, methodology of the United Nations population estimates and projections. Available. https://esa.un.org/unpd/wpp/publications/Files/WPP2012_Methodology.pdf, Accessed date: 21 August 2016.
- Van Vuuren, D.P., Edmonds, J., Kainuma, M., Riahi, K., Thomson, A., Hibbard, K., et al., 2011. The representative concentration pathways: an overview. *Clim. Chang.* 109, 5–31.
- Xia, Y., Ju, Y., Chen, J., You, C., 2014. Hemorrhagic stroke and cerebral paragonimiasis. *Stroke* 45, 3420–3422.
- Yang, G., Wang, Y., Zeng, Y., Gao, G.F., Liang, X., Zhou, M., et al., 2013. Rapid health transition in China, 1990–2010: findings from the Global Burden of Disease Study 2010. *Lancet* 381, 1987–2015.
- Yang, J., Yin, P., Zhou, M., Ou, C.-Q., Guo, Y., Gasparrini, A., et al., 2015. Cardiovascular mortality risk attributable to ambient temperature in China. *Heart* 101, 1966–1972. <http://dx.doi.org/10.1136/heartjnl-2015-308062>.
- Zhao, D., Liu, J., Wang, W., Zeng, Z., Cheng, J., Liu, J., et al., 2008. Epidemiological transition of stroke in China twenty-one-year observational study from the Sino-MONICA-Beijing project. *Stroke* 39, 1668–1674. <http://dx.doi.org/10.1161/STROKEAHA.107.502807>.
- Zhou, M., Wang, H., Zhu, J., Chen, W., Wang, L., Liu, S., et al., 2016. Cause-specific mortality for 240 causes in China during 1990–2013: a systematic subnational analysis for the Global Burden of Disease Study 2013. *Lancet* 387, 251–272. [http://dx.doi.org/10.1016/S0140-6736\(15\)00551-6](http://dx.doi.org/10.1016/S0140-6736(15)00551-6).